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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/585,475	06/02/2000	N. Leigh Anderson	40488	6582

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EXAMINER	
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ART UNIT	PAPER NUMBER
1652	8

DATE MAILED: 03/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/585,475	ANDERSON ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) *14-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The examiner Response to Restriction Requirement, paper No. 7, filed on Feb. 4, 2002. Applicants elected with Group I, claims 1-13. Claim 1-84 are pending in the application. Claims 1-13 are examined on merits. Claims 14-84 are withdrawn from consideration.

DETAILED OFFICE ACTION

1. Restriction/Election

Applicant's election with traverse of Group I, claims 1-13 in Paper No. 7 is acknowledged. Applicants' traverse concerns restriction requirements for claims directed to inventions other than that of Group I, therefore, the traverse is moot with respect to Group I.

The traversal to the other Groups is on the ground(s) that "A search of the genus (independent claim) necessary would include a search of the species (dependent claim). An example would be claims 14 and 15." This is not found persuasive because claim 14 is not a generic claim for dependent claim 15. Claim 15 is directed to toxicity markers of Table 8. Claim 15, although written as dependent on claim 14, is directed to the independent subject matter, toxicity markers of Table 9. However, because claims 14-15 and 20-21 are all directed to toxicity markers, the examiner rejoins Groups II and III into a new Group II. Also, Groups IV and V that are directed to the reagents binding to the toxicity markers are rejoined into Group III that comprises claims 16-17 and 22-23.

The requirement of restriction between the new Groups II and III and Groups VI-XXXII of the previous Office Action (paper No. 5) is still deemed proper and is therefore made FINAL.

Claim 14-84 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

2. Objections

2.1. Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The current title is confusing because it is unknown whether the toxicity is related to protein markers or to pharmaceuticals.

2.1. Specification

The first sentence of the specification is objected to because it is unknown what Applicants mean by the terms efficacy and toxicity.

The specification is objected to because it fails to define the terms toxicity and efficacy.

Alanine aminotransferase is enumerated twice in Table 8. Once as alanine aminotransferase in the forth line, the second time as MSN 204. Tables 8 and 9 are objected to because they contain 115 proteins named only by their

muster spot numbers (MSNs) without referring to the full name of these proteins. Table 9 contains 115 proteins that are already included in Table 8.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware.

3.1. Claims

Claims 5 is objected to for reciting the phrase "as a $p<0.1$". The correct phrase is "at $p<0.01$".

Claim 10 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. The subject matter of claim 10 is contained in lines 9-13 of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 12 is objected to for the use of the language "said proteome is prepared by." A proteome cannot be prepared because it is an internal characteristic of a cell or an organism. A proteome may be visualized or shown by electrophoresis.

3. Rejections

3.1. 35 USC , section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to a method for determining a degree of toxicity or efficacy of an agent, however neither the claims nor the specification define the following terms and phrases:

(a) toxicity,

(b) degree of toxicity ,

(c) markers of toxicity,

(c) efficacy,

(d) markers of efficacy,

(e) to experience toxicity,

(f) to experience an effective response

(g) to experience the degree of such response.

It is also unknown what differs toxicity from efficacy. The claims are, therefore, indefinite.

Furthermore, the term "protein" in line 5 of claim 1 is confusing because it is not clear which protein Applicants refer to; said biological sample contains thousands of proteins. The skilled artisan would not know which particular protein to isolate.

In order to examine claim 1 it is assumed that toxicity or efficacy of an agent is any change it causes in the kind and content (concentration in the

tissue) of the proteins obtained from the exposed tissue as compared to unexposed tissue or the same tissue exposed to an agent for which said changes are already known.

Claims 2 and 3 recite the term "protein toxicity markers" or "the protein efficacy markers" that are not defined by the claims or the specification. It is unclear what Applicant mean by "protein toxicity" or "protein efficacy." For examination purposes it is assumed that Applicants mean toxicity or efficacy markers and any protein from Table 8 or 9 may be used as the marker.

Claims 4 recite the phrase "proteins are increased or decreased" which is confusing. It is not clear whether Applicants mean an increase/decrease in the content of particular proteins in the gel or an increase/decrease of the size/molecular weight of said proteins. For examination purposes it is assumed that Applicants mean an increase/decrease in the content of particular proteins in the gel.

Claim 9 and dependent clam 10 are rejected because claim 9 recites the phrase: "relative amount of toxicity or effectiveness" that is not defined by the claim or specification. Claims 9 and 10 are therefore rendered indefinite.

Claim 11 is rejected as a literary duplicate of claim 10.

3.2. 35 USC section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 and 12-13 are rejected under 35 U.S.C. 102(b) as clearly anticipated by Anderson at al (A two-dimensional gel database of rat liver proteins useful in gene regulation and drug effects studies, *Electrophoresis*, **1991**, 12, 907-903).

The claims are directed to a method for determining toxicity or efficacy of an agent by exposing a tissue in a subject to said agent, extracting proteins from the exposed tissue, measuring levels of protein markers, comparing the levels of the markers with the levels in unexposed tissue or the tissue exposed to a known effective agent (claim 1 and 13), wherein:

- the markers are selected from Table 8, or Table 9 (claims 2 and 3);
- measuring the change in levels of individual proteins in proteome is statistically significant and performed using two-dimensional electrophoresis (claim 4 and 12);
- the statistical significance is at $p<0.01$ or at $p< 0.001$ (claim 5 and 6);
- the agent is a pharmaceutical, particularly antilipemic agent (claim 7 and 8).

Anderson and her co-workers exposed liver tissue in rats to lovostatin or combination of cholestyramine and lovstatin or to none of the chemicals. The animals were sacrificed and livers removed, proteins extracted, and measurements of the levels of protein markers (MSN 413, 993, 1001, 1119, 1250 and 1253 – see Fig.10 and 11 on page 921) was performed in the liver proteome using two-dimensional electrophoresis. Anderson et al used the very method

toward which claim 1 is directed. Their measurements included all the limitations of claims 2-8 and 12-13 because:

- protein marker MSN 413 is quoted in Table 8, and marker MSN 1001 in Table 8 and 9;
- measurements were performed using proteome obtained by two-dimensional electrophoresis;
- the abundance of MSN 413 and MSN 1001 caused by lovostatin or by lovostation and cholestyramine (Fig. 10 and 11 on page 921) may be assessed as statistically significant at $p < 0.01$ or $p< 0.001$;
- lovostatin and cholestyramine are pharmaceuticals and antilipemic agents.

4. Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner